UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/623,472	07/18/2003	Erik Hendrikus, G., M. Boddeke	2183-6042US	4438

24247 7590 08/01/2005

TRASK BRITT
P.O. BOX 2550
SALT LAKE CITY, UT 84110

EXAMINER	
KOLKER, DANIEL E	
ART UNIT	**PAPER NUMBER**
1649	

DATE MAILED: 08/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/623,472	BODDEKE ET AL.	
	Examiner	Art Unit	
	Daniel Kolker	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *11,12 and 14-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 - 10, 13, 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-17* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/18/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's remarks filed 25 April 2005 have been entered. Claims 1 – 17 are pending.

2. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1649.

Election/Restrictions

3. Applicant's election without traverse of Group I (claims 1 – 10, 13, and 17) in the reply filed on 25 April 2005 is acknowledged.

4. Claims 11, 12, and 14 – 16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 25 April 2005.

Priority

5. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in the European Patent Office on 18 January 2001. It is noted, however, that applicant has not filed a certified copy of the 01200181.4 application as required by 35 U.S.C. 119(b). Therefore, priority is set at the date the international application was filed, 18 January 2002.

Specification

6. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see page 14, paragraph 44, for example). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. The objection could be overcome by deleting "http://" from the internet addresses.

Claim Objections

7. Claim 10 is objected to because of the following informalities: it depends from a non-elected claim. For the purposes of examination, the examiner assumes that the claim depends from claim 8 or claim 9. Appropriate correction is required.

8. Claim 13 is objected to because of the following informalities: it has a typographical error ("of inflammatory" should be "or inflammatory"). Appropriate correction is required.

9. Claims 3 – 7 and 9 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 3 recites "wherein the capacity to modulate or mimic MCP-1 binding comprises downregulating the chemokine receptor". Claim 3 depends from claim 1, but fails to limit the parent claim which is drawn to binding, not regulating. Claim 5 is recites the limitation "wherein mRNA expression of said chemokine receptor is up-regulated", but it depends from claim 3, which recites the limitation "wherein the capacity to modulate or mimic MCP-1 binding comprises down-regulating the chemokine receptor". Claims 6 and 7 depend from claim 1, but like claim 3 they do not limit claim 1, as up-regulation of mRNA expression and chemotaxis are not binding. Claim 9 depends from claim 8, but the scope of claim 9, drawn to "at least a functional fragment" of the receptor is broader than that of claim 8, drawn to the entire receptor.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1 – 10, 13, and 17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for providing candidate compounds, does not reasonably provide enablement for testing candidate compounds for their capacity to modulate or mimic binding of MCP-1 to L-CCR, or for identifying compounds that are candidates for treatment of all inflammatory diseases, or for treatment of all degenerative brain diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of

experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (FED. Cir. 1988).

The claims do not require the presence of either MCP-1 or L-CCR in the assay, either in a cell or tissue or provided by the skilled artisan. Claim 1 recites "testing a candidate drug compound for candidate drug compound's capacity to modulate or mimic MCP-1 binding with a receptor". There is not a requirement that anything other than the candidate drug compound be present. The only active step is "testing", but there is not a description of what is encompassed by the term. There is not sufficient guidance to allow the artisan to know what constitutes modulating or mimicking MCP-1 binding, especially when the receptor to which it binds is not present. In order to know whether a compound modulates the binding of MCP-1 to L-CCR, the skilled artisan would have to measure the binding of MCP-1 to L-CCR in the absence of the compound and then measure the binding in the presence of the compound. In order to know whether or not a compound mimics the binding of MCP-1 to L-CCR, the artisan would have to measure the binding between these two, and then measure the binding of the candidate compound to L-CCR. But since there is not a requirement for either MCP-1 or L-CCR to be provided, the recited method will not accomplish the goal stated in the preamble and thus it would take undue experimentation on the part of the artisan to practice the claimed method, as the burden would be upon the artisan to devise the assay.

The specification discloses that not all cell types express L-CCR under all conditions. For example, RAW 264.7 cells only express L-CCR after treatment with LPS (see page 17 paragraph 0051 and Figure 1). Note that there is no expression of L-CCR (also called CCR11) in lane C (control), but it is expressed in the LPS lane of Figure 1. Similarly mouse brain cells do not express L-CCR (also called CCR12, see paragraph 0051) under basal conditions. Page 18, paragraph 0055 clearly states that "no CCR12 mRNA-positive cells were found in control brains." CCR12 mRNA-positive cells were only found following injection of LPS. Furthermore Shimada et al. (1998. FEBS Letters 425:490-494) teach that in most of the cell lines they tested, including 3T3, EL4, 5E3, MOPC, BCL1, and M1, L-CCR is not expressed either before or after treatment with LPS (see Figure 4 from Shimada). Therefore if the method were to be practiced on any of the cultured cells listed above it would not work, with the exception of RAW 264.7 cells that have been treated with LPS, as those are the only cells that express the receptor. While neither Shimada nor the instant specification teach that the L-CCR protein is not expressed in those cell lines, Alberts (1994. Molecular Biology of the Cell) teaches that

transcription is the major control point for protein expression (p. 453) and thus a skilled artisan would expect that there would be no protein in the absence of mRNA expression.

The claims do not require that L-CCR/CCR11/CCR12 be provided. An *in vivo* assay using control mice will not work, as the specification discloses that L-CCR is not expressed in the mouse brain prior to treatment with LPS. Furthermore the art teaches that most cell lines do not express L-CCR (see Figure 4 from Shimada), therefore *in vitro* tests will generally not work. Claim 1 includes the limitation that the L-CCR receptor be capable of being expressed in glia. However the claim does not actually require the presence of glia in general or glia that actually express the receptor in particular. The specification discloses that the receptor usually is not expressed in glia, and is only expressed upon treatment with LPS. The recitation "capable of being expressed on brain glial cells" is not sufficient for enablement, as any chemokine receptor is capable of being expressed exogenously or heterologously on glia.

The claims are very broad, in that they are drawn to methods of identifying candidate compounds for the treatment of all inflammatory diseases and all degenerative brain diseases. The methods steps involve "testing" a candidate drug compound's capacity to either modulate or mimic the binding of MCP-1 to a chemokine receptor know as either L-CCR or CRAM-B. There is no guidance in the specification as to what constitutes "testing" The specification (p. 4, paragraph 6) discloses that this receptor is also known as CCR11 and CCR12. Furthermore dependent claims 3 and 5 recite the terms "down-regulating" and "up-regulated" respectively. These terms are broad in that they include changes in the amount of mRNA, protein, and activity of the protein.

The specification discloses (p. 3, paragraph 5) that monocyte chemoattractant protein-1 (MCP-1) is a chemokine ligand for CCR12, and that incubation of microglia or astrocytes with MCP-1 induces intracellular calcium and/or chemotaxis. This is in agreement with the prior art (see for example Schweickart et al. 1999. Journal of Biological Chemistry 275:9550-9556, who teach that MCP-1 induces chemotaxis and Boddeke et al. 1999 Journal of Neuroimmunology 98:176-184 who teach that MCP-1 induces intracellular calcium). Furthermore, the specification discloses that incubation of cultured microglia and astrocytes with lipopolysaccharide (LPS) induces expression of CCR12 mRNA (figure 4, specification p. 10, paragraph 26). Again, this is in agreement with the prior art, as Shimada et al. teach that LPS treatment increases the amount of L-CCR mRNA in cells.

The specification discloses that upon intraperitoneal injection of LPS, expression of CCR12 mRNA is increased (p. 18). The specification provides a working example (pp. 24 – 26) which shows that CCR11 mRNA is induced in experimental autoimmune encephalitis, an art-recognized model of multiple sclerosis, in which myelin oligodendrocyte protein was used as the antigen. However, there are no data to support the conclusion that an agent which mimics MCP-1 binding to CCR11 is a candidate for the treatment of either inflammatory or degenerative brain diseases, or even the more limited conclusion at the end of paragraph 64 (p. 26) that MCP-1 antagonists are useful in the treatment of multiple sclerosis. Multiple sclerosis is characterized by a loss of myelin, not by a disorder of chemokine signaling.

Furthermore, the specification discloses that administration of aerosolized ovalbumin to mice sensitized to the same antigen induces MCP-1 and CCR11 mRNA at one hour, and that it induces MCP-1 at 3 and 6 hours after antigen presentation. This finding is not sufficient to support the conclusion that an agent which mimics MCP-1 binding to CCR11 is a candidate for the treatment of either inflammatory or degenerative brain diseases, or even the more limited conclusion that such an agent is useful in treating chronic obstructive pulmonary disease.

The working examples in the disclosure are drawn to measurement of mRNA of either CCR11 or CCR12 (the terms are used synonymously; see p. 4) either directly by in situ hybridization or indirectly by RT-PCR. The prior art teaches that transcription of mRNA from genomic DNA is complex, and that it can be affected by many factors. Alberts et al. (1994. Molecular Biology of the Cell, pp. 417 – 433) teach that there are many factors that affect transcription, including a host of regulatory proteins, general transcription factors, and 3' regulatory proteins (see Figure 9-34, page 424 in particular). The working examples in the specification indicate that administration of certain antigenic proteins (e.g. LPS or ovalbumin) induces either CCR11 or MCP-1 mRNA does not reasonably support the conclusion that MCP-1 binding to CCR11 is a cause of inflammatory disease or degenerative brain disease. The working example purporting to provide support for the use of screening assays to find candidate drugs for chronic obstructive pulmonary disease (COPD; pp. 26 - 29) is particularly informative. MCP-1 mRNA is increased at 1, 3, and 6 hours after allergen provocation, but CCR11 mRNA is only "slightly increased at one hour", and is not increased at all at other time points. Clearly if MCP-1 induction of CCR11 mRNA causes inflammatory disease, CCR11 mRNA would have been elevated at all time points when MCP-1 was elevated. Furthermore, there is not a causative link between CCR11 and inflammation, either in the art or in the specification. In fact,

the post-filing publication by Zuurman et al. (2003. Glia 41:327-336) characterizes the association between inflammation and L-CCR as a subject worthy of speculation (see p. 336, final paragraph), but speculation is not enablement. Claim 9 is drawn to "at least a functional fragment" of L-CCR or CRAM-B, but the specification does not disclose which fragments are functional, or how to determine which fragments are functional.

Furthermore, the specification is not enabling for the discovery of agents which are reasonably construed as candidates for all inflammatory diseases or all degenerative brain diseases. The art teaches that IL-1 beta and TNF-alpha are involved in arthritis, which is an inflammatory disease (see Chikanza et al., 2000. Exper Opin Investig Drugs 9:1499-1510), but a skilled artisan would not immediately recognize that compounds identified through the assays presented here are useful as candidates in the treatment of arthritis. The genus of inflammatory diseases are not all related to CCR11 or MCP-1, and therefore the instantly-claimed methods are not enabled for finding candidate compounds for treatment of all inflammatory diseases. Similarly, not all degenerative brain diseases are influenced by inflammation or by CCR11. For example, Parkinson's disease is characterized by the death of dopaminergic neurons, not inflammation, and schizophrenia is known to lead to increased ventricle size and a corresponding decrease of brain tissue. Therefore the specification cannot be considered enabling for all degenerative brain diseases, as it will not identify compounds useful as candidates in treatment of all degenerative brain diseases.

The claims are drawn to methods of identify compounds by testing a compound's ability to either modulate or mimic MCP-1 binding. It is unclear what would constitute a mimicking of the binding. A skilled artisan would not be able to tell if a compound "mimics" the binding of MCP-1 to the receptor, since the term is not well-defined in the specification. It is unclear whether binding to the receptor without activating a calcium transient would constitute mimicking the binding of MCP-1. Additionally, since the working examples present data which suggest that CCR11 mRNA is increased during disease states, and the specification discloses that MCP-1 induces CCR11 mRNA, it is unclear how a compound which mimics MCP-1 binding could reasonably be construed as a candidate for a treatment of a disease, as it would tend to exacerbate, not ameliorate the symptoms. Therefore the specification is not deemed enabling for identifying drugs which are candidates for the treatment of inflammatory or degenerative brain diseases, as a skilled artisan would recognize that many of the compounds identified by the assay (i.e. those that increase the effects of MCP-1 or mimic its binding) would be expected

to exacerbate the symptoms of the disease. Claim 3 defines modulating or mimicking the activity of MCP-1 binding as comprising "down-regulating the chemokine receptor". But the specification discloses that MCP-1 binding activates (i.e. up-regulates) the chemokine receptor (see p. 4, paragraph 6).

Claim 5 is not considered enabled over its full scope because not all compounds which mimic or modulate binding of MCP-1 to the chemokine receptor will result in an increase of the receptor. For example, if MCP-1 increases amount of L-CCR mRNA, then an antibody which binds to MCP-1 will modulate MCP-1 binding by decreasing it, will not increase the mRNA level.

Claim 17 is drawn to a screening method comprising testing a drug for the drug's ability to "down-regulate" the chemokine receptor. A skilled artisan would not be able to perform the method as claimed, because the method does not require the presence of the receptor. Furthermore the claim is very broad. Down-regulating is not explicitly defined in the specification. The broadest reasonable interpretation of "down-regulate" includes a decrease of mRNA, or of protein, or of the activity of the receptor in the absence of any change in either mRNA or protein. Applicant has not demonstrated what the activity of the receptor is, and therefore the artisan certainly could not tell if the activity is down-regulated. Additionally, applicant has not provided any examples, either working or prophetic, of candidate drug compounds that have the capacity to down-regulate the receptor. Given the lack of working examples, the breadth of the claim, the complex nature of the invention, and the lack of guidance provided by the specification, it would take undue experimentation on the part of a skilled artisan to practice the method of claim 17 over its full scope.

12. Claims 1 – 10, 13, and 17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to methods of determining if a candidate compound modulates of mimics binding of MCP-1 to L-CCR or CRAM-B. Applicant has not described compounds that modulate the binding of MCP-1 to the receptor, nor has applicant described compounds that mimic the of MCP-1 to the receptor. There is not a disclosure of how to determine what constitutes mimicking of the binding of MCP-1 to the receptor. Furthermore, there is not a disclosure of the full scope of the functional effects of the binding of MCP-1 to the receptor.

Additionally, the only active step recited in the claimed methods is "testing" but applicant has not described what constitutes testing. Since applicant has not described these effects, the artisan would not know how to determine if the binding of MCP-1 to the receptor had been modulated.

Furthermore claim 9 is drawn to "at least a functional fragment" of L-CCR or CRAM-B, but the specification does not disclose what fragments constitute functional fragments. One of skill in the art would not be able to know, based on the disclosure, which elements are necessary to carry out the assays claimed herein.

Claim 17 is drawn to testing a compounds capacity to "down-regulate" the receptor. Applicant has not described what it mean for a compound to have the capacity to down-regulate the receptor. This term could mean decreasing the amount of mRNA that encodes the receptor, or decreasing the amount of the receptor, or it could mean decreasing the activity of the receptor, but applicant has not described the activity of the receptor. Furthermore applicant has not described any compounds which down-regulate the receptor.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision how to carry out the assays, or the detailed chemical structure of the compounds that would be identified in the assay, and therefore conception is not achieved until reduction to practice has occurred. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 1 – 10, 13, and 17 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the MCP-1 and L-CCR proteins. As described in detail on p. 4 of this office action, the presence of MCP-1 and L-CCR

would appear to be required for the practice of the methods, but they are not required in the claims.

15. Claims 1 – 10, 13, and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The only active step recited in claims 1 and 17 is "testing". Claim 13 recites both "testing" and "determining". But in neither case is there sufficient disclosure of what constitutes "testing" to allow an artisan to determine the metes and bounds of the claims.

Claims 3 – 7 are drawn to down-regulating (claim 3), upregulating (claims 5 – 6), and chemotaxis (claim 7). These are effects which are physiological and biochemical changes in a cell, and are not "binding" as recited in claim 1. The effects are unrelated to binding and can occur in cells in the absence of any binding. A skilled artisan would not be able to determine the metes and bounds of the claims, because these dependent claims are not proper limitations of the parent claim. Additonally, it is unclear what is meant by the terms up-regulated and down-regulated. These terms could mean a change in the amount of the receptor, or in the mRNA encoding the receptor, or in an undisclosed activity of the receptor. Because these terms are ambiguous and not explicitly defined in the specification, a skilled artisan would not be able to determine the metes and bounds of the claims.

Claim 5 recites the limitation "wherein mRNA expression of said chemokine receptor is up-regulated", but it depends from claim 3, which recites the limitation "wherein the capacity to modulate or mimic MCP-1 binding comprises down-regulating the chemokine receptor". It is not clear how the method can detect both down-regulation of the chemokine receptor and up-regulation of the mRNA encoding the receptor, therefore the claim is indefinite.

Claim 5 recites the limitation "mRNA expression" in the first line. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Applicant is reminded that priority to the EPO application has not been granted, since a certified copy of the foreign priority document was not provided. Therefore the effective filing date of the instant application is the date the international was filed, 18 January 2002.

17. Claims 1 - 2, 7 – 9, and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Schweickart et al. (2000. Journal of Biological Chemistry 275:9550-9556, cited on IDS). Schweickart et al. teach screening 29 cytokines for their ability to induce chemotaxis in cells expressing CCR11 (see p. 9552, top of second column). The specification teaches that CCR11 is a synonym for L-CCR (see page 4 line 4 and page 9 line 8). Schweickart et al. teach comparing the ability of candidate compounds to mimic the effects of MCP-1 in the chemotaxis assay (see figure 5, for example), thereby fairly meeting the limitations of "testing" and "determining" recited in claims 1 and 13. Shweickart et al. teach chemotaxis assays, meeting the limitation of claim 7, and recombinant cultured cells expressing the nucleic acid encoding CCR11 (see p. 9551, first column, "CCR11 expression" and "Chemotaxis assays"), meeting the limitations of claims 8. Claim 9 is drawn to "at least a functional fragment" of the receptor, but since Schweickart teaches the complete receptor this necessarily includes functional fragments, and thus meets the limitation of claim 9. The recitation "for the treatment of an inflammatory or degenerative brain disease" (claim 1), enumeration of specific conditions (claim 2), and recitation of "degenerative or inflammatory disease" are intended uses of the compounds and are not given patentable weight.

18. Claims 1 – 2, 7 – 10, and 13 are rejected under 35 U.S.C. 102(e) as being anticipated by Gray et al. (WO 01/66598, cited on IDS, published 13 September 2001, filed 5 March 2001, claiming priority to provisional applications filed 3 March 2000). Gray et al. teach assays to identify modulators of CCR11 activity (see pages 66 – 76). Specifically they teach expressing HEK cells with a nucleic acid encoding CCR11 (p. 67), and screening candidate compounds for their ability to bind to CCR11. Gray teaches direct assays for ligands (p. 67) and indirect assays for ligands (p. 68 - 76), including GTP hydrolysis assay (p. 68) GTP-gamma-S binding assay (pp. 68 – 70), cAMP assays (pp. 70 – 71), intracellular calcium assays (p. 71 – 73), phospholipase C assays (p. 73) arachadonic acid release assays (p. 74), extracellular

acidification assays (p. 74 – 75), chemotaxis assays (p. 75), and competition binding assays (pp. 75 – 76), all of which are sufficient to identify compounds which are ligands of CCR11. The specification provides evidence that MCP-1 is a ligand for CCR11, therefore Grey's assays are inherently assays for compounds that mimic MCP-1 binding. Thus the teachings of Grey fairly meet the "testing" and "determining" limitations of claims 1 and 13. The recitation "for the treatment of an inflammatory or degenerative brain disease" (claim 1), enumeration of specific conditions (claim 2), and recitation of "degenerative or inflammatory disease" are intended uses of the compounds and are not given patentable weight. Since Grey explicitly teaches chemotaxis assays (p. 75), and HEK cells expressing the receptor, the teachings fairly meet claims 7, 8, and 10. Claim 9 is drawn to a cell expressing at least a functional fragment of the receptor. Since Grey teaches cells expressing the entire receptor, the teachings also anticipate claim 9.

19. Claims 1 – 2 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Gish et al. (WO 98/01557, published 15 January 1998). Gish et al. teach SEQ ID NO:12; bases 85 – 1119 of their SEQ ID NO:12 are identical to applicant's SEQ ID NO:31, which is identified as human CCR12 (see enclosed alignment). Gish et al. teach kits comprising the protein encoded by this nucleic acid, and use of the kits to screen for the binding affinity of a test compound (see page 46 lines 11 – 33). Gish further teaches particular methods of performing the assays (see pp. 48 – 49). Since the binding affinity of MCP-1 for its receptor is one of its inherent properties, and since Gish et al. teach screening for agents which have "suitable binding affinity" and determining whether those agents act as agonists or antagonists on the receptor (see p. 46 line 30), Gish inherently teaches screening for agents which mimic MCP-1 binding. Thus the teachings of Gish fairly meet the "testing" and "determining" limitations of claims 1 and 13. The recitation "for the treatment of an inflammatory or degenerative brain disease" (claim 1), enumeration of specific conditions (claim 2), and recitation of "degenerative or inflammatory disease" are intended uses of the compounds and are not given patentable weight.

20. Claims 1, 2, 8, and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Boddeke et al. (1999. Journal of Neuroimmunology 98:176-184) as evidenced by Dorf and by Schweickart. Boddeke teaches testing RANTES and MIP-1α to produce calcium transients similar to MCP-1 (see p. 182, Figure 4, and Figure 6). It is acknowledged that Boddeke et al. do not teach expression of L-CCR/CCR11/CCR12 in their cells. However, Boddeke used cultured rat microglia treated with LPS (see legend for Figure 6), and the specification provides evidence

that stimulation of microglia with LPS is sufficient to induce expression of L-CCR as claimed. Since the method constitutes "testing" for compounds that mimic the effect of MCP-1 and was performed on cells that express the receptor, the reference fairly teaches the screening methods of claims 1 and 13. The recitation "for the treatment of an inflammatory or degenerative brain disease" (claim 1), enumeration of specific conditions (claim 2), and recitation of "degenerative or inflammatory disease" are intended uses of the compounds and are not given patentable weight. The methods taught by Boddeke used cultured cells, specifically microglia (see p. 178, "Microglia cultures"), meeting the limitation of claim 8.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel Kolker whose telephone number is (571) 272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel E. Kolker, Ph.D.
July 19, 2005

Brenda Brumback
BRENDA BRUMBACK
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600